Agenesis of maxillary lateral incisors and associated dental anomalies

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Introduction: The objectives of this study were to evaluate the prevalence of dental anomalies in patients with agenesis of maxillary lateral incisors and to compare the findings with the prevalence of these anomalies in the general population. Methods: A sample of 126 patients, aged 7 to 35 years, with agenesis of at least 1 maxillary lateral incisor was selected. Panoramic and periapical radiographs and dental casts were used to analyze other associated dental anomalies, including agenesis of other permanent teeth, ectopia of unerupted permanent teeth, microdontia of maxillary lateral incisors, and supernumerary teeth. The occurrence of these anomalies was compared with prevalence data previously reported for the general population. Statistical testing was performed with the chi-square test (P < 0.05) and the odds ratio. Results: Patients with maxillary lateral incisor agenesis had a significantly increased prevalence rate of permanent tooth agenesis (18.2%), excluding the third molars. The occurrence of third-molar agenesis in a subgroup aged 14 years or older (n = 76) was 35.5%. The frequencies of maxillary second premolar agenesis (10.3%), mandibular second premolar agenesis (7.9%), microdontia of maxillary lateral incisors (38.8%), and distoangulation of mandibular second premolars (3.9%) were significantly increased in our sample compared with the general population. In a subgroup of patients aged 10 years or older (n = 115), the prevalence of palatally displaced canines was elevated (5.2%). The prevalences of mesioangulation of mandibular second molars and supernumerary teeth were not higher in the sample. Conclusions: Permanent tooth agenesis, maxillary lateral incisor microdontia, palatally displaced canines, and distoangulation of mandibular second premolars are frequently associated with maxillary lateral incisor agenesis, providing additional evidence of a genetic interrelationship in the causes of these dental anomalies. (Am J Orthod Dentofacial Orthop 2010;137:732.e1-732.e6)

Tooth agenesis is the most common dental abnormality, and genetics play a fundamental role in its etiology. The various clinical manifestations of tooth agenesis reflect the genetically and phenotypically heterogeneity of this condition. Molecular genetics have shown mutations in MSX1, PAX9, and AXIN2 in families with multiple dental agenesis. Additionally, mutations in many other genes have been identified in syndromes and congenital abnormalities in which tooth agenesis is a regular feature.

Tooth agenesis is frequently associated with other dental anomalies such as microdontia, delayed dental development, and some discrete tooth ectopias. These dental anomalies commonly appear together in the same patient; the possible explanation is that a certain genetic mutation might cause a series of different phenotypic expressions. In other words, different dental anomalies in the same subject could be distinctive expressions of the same genetic code.

Garn et al and Garn and Lewis were the first investigators to identify a pattern of associated dental anomalies. They found that patients with third molar agenesis had an increased prevalence of agenesis of other permanent teeth, as well as a general reduction in tooth size and delayed dental development. The agenesis of second premolars was also associated with higher prevalences of agenesis of other permanent teeth, microdontia of maxillary lateral incisors, infraocclusion of mandibular deciduous molars, and some types of ectopic eruptions. Palatally displaced maxillary canines, distoangulation of mandibular second premolars, ectopic eruption of maxillary first molars, mesioangulation of mandibular
second molars, and some types of tooth transpositions are dental ectopias frequently associated with second premolar agenesis.\textsuperscript{9,11,13,14}

In addition to third molars and second premolars, maxillary lateral incisors have a high prevalence rate of agenesis.\textsuperscript{17} Although previous studies reported an association between maxillary lateral incisor agenesis and tooth transpositions,\textsuperscript{13} palatally displaced canines (PDC),\textsuperscript{16} and premolar rotations,\textsuperscript{18} no study has evaluated the frequency of associated dental anomalies in a large sample of subjects with maxillary lateral incisor agenesis compared with reference values.

Therefore, in this study, we aimed to determine the prevalence of permanent tooth agenesis, discrete ectopias, microdontia, and supernumerary teeth in patients with agenesis of the maxillary lateral incisors, comparing these prevalences with those in the general population. The hypothesis was that subjects with agenesis of maxillary lateral incisors have significantly increased prevalences of other dental anomalies.

\section*{MATERIAL AND METHODS}

A sample of 126 subjects with agenesis of the maxillary lateral incisors was selected from the orthodontic patient files of the University of São Paulo City in Brazil and some private dental offices in Brazil. The subjects ranged in age from 7 to 35 years, and there were 84 female and 42 male subjects, with a sex ratio of 2:1. Because of the widely heterogeneous backgrounds of Brazilians, a rough estimate of the ethnic makeup of the sample was derived subjectively from facial photographic records: white (80\%) and black mixture (20\%). No Asian subjects were included in the sample. Panoramic radiographs, periapical radiographs, and dental casts were used to investigate these dental anomalies: agenesis of permanent teeth; supernumerary teeth; microdontia of maxillary lateral incisors; and 3 types of tooth ectopia including PDC, distal angulation of mandibular second premolars, and mesial angulation of mandibular second molars.

The critical age of 14 years was considered to confirm the absence of third molars.\textsuperscript{5} This criterion was used to restrict the sample for evaluation of third-molar agenesis to only those with diagnostic records at 14 years of age or older (n = 76). Diagnosis of palatally displaced maxillary canines followed the radiographic parameters suggested by Lindauer et al.,\textsuperscript{19} and it was confirmed by interpretation of periapical radiographs by the tube-shift technique, a method of object localization with 2 projections with significantly different x-ray tube angulations. Taking into account the findings of Ericson and Kurol\textsuperscript{20} that the attempt to determine the eruption path of maxillary canines radiographically is generally of little value in children younger than 10 years, only subjects 10 years of age or older were considered in evaluating PDC (n = 115). Diagnosis of distal angulation of mandibular second premolars followed the criteria of Shalish et al.,\textsuperscript{12} using the inferior border of the mandible as a baseline. The maxillary lateral incisor was considered as having microdontia when the maximum mesiodistal crown diameter was smaller than the same dimension of the opposing incisor in the same patient.\textsuperscript{14} This category also included conical and peg-shaped maxillary lateral incisors.

\section*{RESULTS}

In the sample of 126 patients with agenesis of maxillary lateral incisors, 51.6\% (n = 65) had bilateral expression, and 27.7\% (n = 35) had right unilateral and 20.7\% (n = 26) had left unilateral expression.

The prevalence of other permanent tooth agenesis in the sample, excluding third molars, was 18.2\%, a 3-fold increased prevalence (OR, 3.5) compared with reference values in the general population (Table I). The frequencies of maxillary second premolar (OR, 7.5), mandibular second premolar (OR, 2.7), and mandibular third molar (OR, 2.0) agenesis were significantly higher in the sample compared with the general population (Table I). No differences between the sample and the reference values were observed for the prevalence of supernumerary teeth (Table I).

Patients with agenesis of maxillary lateral incisors showed a significantly higher prevalence of microdontia...
of maxillary lateral incisors (OR, 12.9), as shown in Table II. Considering only the patients with unilateral agenesis of maxillary lateral incisors (n = 61), 80.3% (n = 49) had a size reduction of the contralateral tooth.

The prevalences of PDC and distal angulation of mandibular second premolars were significantly increased in the sample compared with the general population: 5.2% (OR, 3.1) and 3.9% (OR, 20.8), respectively (Table II). In contrast, no difference was observed for the frequency of mesial angulation of mandibular second molars in the sample compared with the reference values (Table II).

**DISCUSSION**

We analyzed the associations between missing maxillary lateral incisors and other tooth disturbances in a large sample of subjects using reference data from control population groups. These comparison data came from studies with samples more homogeneous racially and ethnically than our sample. Previous investigations, however, showed small differences among ethnicities or racial groups in the general frequencies of some dental anomalies observed in this study. Also, much of the reference data derives from orthodontic patients before treatment, when the prevalence rates for dental anomalies could be different from those of subjects not screened for orthodontic needs. In spite of this, the main purpose of this study was to verify the association between dental anomalies; our methodology was used previously in many other investigations.

In the sample of subjects with agenesis of maxillary lateral incisors, the frequency of agenesis of other permanent teeth was significantly higher (Table I). The prevalence of other missing permanent teeth, excluding third molars, was 18.2% (OR, 3.5). Interestingly, among the patients with agenesis of other permanent teeth (n = 23), 73.9% (n = 17) had bilateral expression of maxillary lateral incisor agenesis. Therefore, considering only the subsample of patients with bilateral agenesis of maxillary lateral incisors (n = 65), the frequency of
associated permanent tooth agenesis was 26.1%. In other words, a quarter of the patients with bilateral lateral incisor absence were missing other permanent teeth, excluding the third molars. The more severe expression of the phenotype represented by missing lateral incisors was therefore concurrent with the higher prevalence of other missing teeth in the same subjects, thus indicating a strong level of expressivity of the related genotype.

When we analyzed the complete sample, all categories of permanent teeth could be absent, with the exceptions of the maxillary and mandibular first molars. The maxillary second premolar followed by the mandibular second premolar were the most frequently absent teeth with a 7-fold and 2.5-fold increased prevalence compared with general population, respectively. In a subgroup of patients older than 14 years, the prevalence of third molar agenesis was significantly higher (35.5%) compared with the reference values (Table I).

Garib et al14 observed that 21% of the patients with second premolar agenesis had microdontia of maxillary lateral incisors.5 Specifically concerning the maxillary lateral incisor, the prevalence of agenesis in the study group was 12%, compared with 1.2% in the control group.5 Garib et al14 observed that 21% of the patients with second premolar agenesis had other permanent teeth missing, excluding the third molars, a 4-fold increased prevalence compared with the general population. All dental groups were affected, but the maxillary lateral incisor was the most commonly absent teeth, with an 8-fold increased frequency of agenesis (16.3%) compared with the reference values (1.9%).14 Our study showed an association between different permanent tooth agenesis; this agrees with the results of Garn and Lewis5 and Garib et al.14 The possible explanation is that 1 gene mutation might interfere in the morphogenesis of more than 1 group of teeth. Studies of families and investigations of the association of agenesis and other dental anomalies previously highlighted the role of genetic mechanisms in the etiology of tooth agenesis.7,9,11,13,15,16,23,27

Unlike tooth agenesis, the prevalence of supernumerary teeth in our sample was not statistically different from that of the general population (Table I). This suggests that these anomalies have different or independent etiologic factors. This is understandable, considering that tooth agenesis is a hypoplastic dental anomaly, whereas supernumerary teeth are hyperplastic anomalies. These results corroborate the findings of Baccetti11 and Garib et al,14 who did not find higher frequencies of supernumerary teeth in samples with second premolar agenesis.

The unilateral agenesis of the maxillary lateral incisor and microdontia of its antimere represent a classic association of dental anomalies in the literature.28 In this study sample, the prevalence of maxillary lateral incisor size reduction was 38.8% (OR, 12.9), an 8-fold increased prevalence compared with the reference values (Table II). In reality, considering only the subsample with unilateral maxillary lateral incisor agenesis, contralateral size reduction was observed in 80.3% of the patients. These results are in agreement with previous studies pointing out that tooth agenesis and microdontia are different expressions of the same genetic defect once these phenotypes appear associated.6,28,29 Garn and Lewis6 observed a general reduction in tooth size in patients with third molar agenesis. This reduction was even more remarkable in patients with oligodontia. Brook29 analyzed families of patients with dental anomalies and observed that agenesis and microdontia often occur concomitantly. Baccetti11 also obtained similar results, demonstrating that 18% of patients with agenesis of second premolars had microdontia of maxillary lateral incisors, and nearly half of patients with small maxillary lateral incisors (42%) had agenesis of second premolars. Garib et al14 found that approximately 20% of the patients with second premolar agenesis also had maxillary lateral incisor microdontia. These findings have clinical relevance in orthodontics. A treatment plan that includes replacement of the missing lateral incisor in patients with unilateral agenesis of the maxillary lateral incisor should consider augmentation of its antimere to obtain a balanced and symmetrical smile.

The prevalence of PDC in the sample was 5.2%, a 3-fold increased prevalence (OR, 3.1) compared with the general population (Table II). Among the 6 patients identified, 5 had unilateral PDC, and 1 had bilateral occurrence, for a total of 7 ectopic maxillary canines. The ectopic eruption toward the palate coincided with the same quadrant of maxillary lateral incisor agenesis for all maxillary canines, except one that was observed at the side of a small maxillary lateral incisor. Conversely, in a sample of 19 patients with a phenotype associating unilateral expression of maxillary lateral incisor agenesis and PDC, Becker et al30 found that canine ectopia occurred more frequently on the side of the small lateral incisor than on the side of the lateral incisor agenesis.

Previous studies have shown frequent associations of PDC with second premolar agenesis, third molar agenesis, microdontia of maxillary lateral incisors, and infraocclusion of deciduous molars.9,11,13,14 In
accordance with our study, Sacerdoti and Baccetti\textsuperscript{16} reported an increased prevalence of PDC (20\%) in a sample of subjects with maxillary lateral incisor agenesis (n = 40), compared with a control group. However, the reciprocal association was not found in investigations of the prevalence of maxillary lateral agenesis in subjects primarily selected with PDC.\textsuperscript{9,13,16} A significant increased prevalence of maxillary lateral incisor agenesis (18.9\%) was found only for subjects with unilateral expression of PDC.\textsuperscript{16}

Currently, 2 theories explain the occurrence of the PDC anomaly. Becker et al\textsuperscript{31,32} proposed that local factors such as agenesis and microdontia of maxillary lateral incisors are the major etiologic factors of maxillary canine ectopic eruption. Based on the “guidance theory of canine palatal displacement,” the roots of maxillary lateral incisors work as guides for maxillary canine eruption.\textsuperscript{33} Without a maxillary lateral incisor or with an anomalous root morphology, a maxillary canine could develop an ectopic eruption path.\textsuperscript{33} This theory, however, can explain only approximately 20\% of PDC cases.\textsuperscript{33} Another explanation for PDC occurrence is the genetic theory.\textsuperscript{8} Peck et al\textsuperscript{8} compiled some evidence of the genetic etiology of PDC including concomitant occurrence with other genetic anomalies such as tooth agenesis, frequent familial history, and differences in the prevalences observed for the sexes and different populations. Under this light, maxillary lateral incisor agenesis and PDC might share a common genetic background. These data have clinical relevance since absence of maxillary lateral incisors might be an early risk indicator for PDC development. However, considering the prevalence rate of PDC associated with other dental anomalies, maxillary lateral incisor agenesis is weaker as a risk indicator for PDC than second premolar agenesis, maxillary lateral incisor microdontia, and infraocclusion of deciduous molars. Therefore, these results, in addition to the data of Sacerdoti and Baccetti,\textsuperscript{16} do not support the guidance theory, because the most severe expression of a presumed “lack of guidance” for the erupting canine offered by the lateral incisor (absence of the incisor) has a smaller association value with PDC than anomalies in regions of the dental arch distant from the canine.

The ectopic eruption of mandibular second premolars toward the distal aspect seems to be a mild expression of the same genetic base that determines second premolar agenesis. Symons and Taverne\textsuperscript{34} observed the distoanangement of mandibular second premolar buds in a family with multiple agenesis including the second premolars. Shalish et al\textsuperscript{12} demonstrated that patients with unilateral agenesis of mandibular second premolars often exhibit distal angulation and delayed development of the unerupted contralateral second premolar. Garib et al\textsuperscript{14} found a higher prevalence of mandibular second premolar distoanangement (7.9\%) in a sample of patients with second premolar agenesis compared with the prevalence expected in the general population (0.2\%). Our results showed that 4\% of the patients with maxillary lateral incisor agenesis have distoanangement of mandibular second premolars, a 20-fold increased prevalence (OR, 20.8) compared with the reference values (Table II). Among the 5 patients in the sample with ectopic eruption of mandibular second premolars, just 2 had agenesis of second premolars. Distoanangement of mandibular second premolars is usually mild and self-corrects during tooth eruption.\textsuperscript{12} Therefore, our methodology might have underestimated this prevalence because the ages of the subjects with mandibular second premolar distoanangement varied from 9 to 15 years, whereas the complete sample had a wider age range. Patients examined in the third decade of life usually had fully erupted mandibular second premolars.

Impaction of mesially angulated mandibular second permanent molars is a rare eruption disturbance affecting 0.06\% of the population\textsuperscript{24}; the etiology is frequently assigned to local factors, such as a deficient dental arch perimeter.\textsuperscript{35} Not all cases of retention of mandibular second molars can be assigned to local causes, such as deficient dental arch space and mechanics involving distalization of mandibular first molars. In some patients, a normally developing tooth bud of a mandibular second molar might in a short time change its angulation to a significant mesial inclination, without apparent cause, thus remaining impacted on the distal aspect of the mandibular first molar.\textsuperscript{35} Garib et al\textsuperscript{34} observed an increased prevalence of mesioanangement of mandibular second molars (1\%) in a sample of patients with second premolar agenesis compared with the prevalence reported for the general population. Differently, no cases of mesial angulation of mandibular second molars were found in our study sample. Therefore, no association between agenesis of maxillary lateral incisors and mesial angulation of mandibular second molars could be established.

This study highlights the importance of genetics with associated dental anomalies. With the advances in molecular biology, future diagnostic tools for prevention of some dental anomalies might include genetic mapping.

**CONCLUSIONS**

The hypothesis that subjects with maxillary lateral incisor agenesis demonstrate increased prevalence of other dental anomalies was corroborated. There was
a significant association between agenesis of maxillary lateral incisors and agenesis of other permanent teeth, as well as increased occurrence of microdontia of maxillary lateral incisors, palatal displacement of canines, and distal angulation of mandibular second premolars. These associations can be explained by a previously postulated genetic interrelationship in the causes of these dental anomalies.

REFERENCES